

3. (Twice Amended) A combinatorial library of different sequence peptide or peptidomimetic members synthesized in solution, where each constituent library member comprises:

C (a) a peptidomimetic sequence of a combination of three or more amino acid residues and mimics of amino acid residues characterized by (i) a sequence of two or more amino acid residues, mimics of amino acid residues or combinations thereof forming a metal ion-binding domain and including at least one amino acid residue or mimic of an amino acid residue containing at least one S wherein the said S is protected by an orthogonal S-protecting group, the orthogonal S-protecting group being compatible with peptide synthesis in solution and removable without cleaving or otherwise altering the peptidomimetic sequences, (ii) a sequence of one or more amino acid residues, mimics of amino acid residues or combinations thereof at either the N- or C- terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain, provided that the at least one amino acid residue containing at least one S protected by an orthogonal S-protecting group is not the terminal amino acid at either the N- or C-terminus, and

(b) a unique selection or sequence of amino acid residues, mimics of amino acid residues or combinations thereof in the peptidomimetic sequence of at least one of the constituent members of the library.

#### REMARKS

The foregoing amendment is being offered to correct a typographic error. Sequences synthesized in solution are not, a priori, bound to solid phase. See also the specification at pages 16-17 and 20-21, discussing library strategies, including solution phase synthesis.


Authorization is given to charge payment of any additional fees required to Deposit Account 13-4213.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached paper is captioned "Version with Markings to Show Changes Made."

Should the Examiner have any queries, suggestions or comments relating to a speedy disposition of the application, the Examiner is invited to call the undersigned.

Entry of this amendment by the Examiner is respectfully requested, as well as consideration and allowance of the application.

Respectfully submitted,  
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3. (Twice Amended) A combinatorial library of different sequence peptide or peptidomimetic members synthesized in solution, where each constituent library member comprises:

(a) a peptidomimetic sequence of a combination of three or more amino acid residues and mimics of amino acid residues [bound to solid phase] characterized by (i) a sequence of two or more amino acid residues, mimics of amino acid residues or combinations thereof forming a metal ion-binding domain and including at least one amino acid residue or mimic of an amino acid residue containing at least one S wherein the said S is protected by an orthogonal S-protecting group, the orthogonal S-protecting group being compatible with peptide synthesis in solution and removable without cleaving or otherwise altering the peptidomimetic sequences, (ii) a sequence of one or more amino acid residues, mimics of amino acid residues or combinations thereof at either the N- or C- terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain, provided that the at least one amino acid residue containing at least one S protected by an orthogonal S-protecting group is not the terminal amino acid at either the N- or C-terminus, and

(b) a unique selection or sequence of amino acid residues, mimics of amino acid residues or combinations thereof in the peptidomimetic sequence of at least one of the constituent members of the library.

The invention further provides a combinatorial library of different sequence peptidomimetic members synthesized on solid phase, where each constituent library member includes (a) a peptidomimetic sequence of a combination of three or more amino acid residues and mimics of amino acid residues bound to solid phase characterized by (i) a sequence of two or more amino acid residues, mimics of amino acid residues or combinations thereof forming a metal ion-binding domain and including at least one amino acid residue or mimic of an amino acid residue containing at least one S wherein the said S is protected by an orthogonal S-protecting group, (ii) a sequence of one or more amino acid residues, mimics of amino acid residues or combinations thereof at the N- or C- terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain, and (iii) a cleavable bond attaching the peptidomimetic sequence to solid phase; and (b) a unique selection or sequence of amino acid residues, mimics of amino acid residues or combinations thereof in the peptidomimetic sequence of at least one of the constituent members of the library. In this library, the orthogonal S-protecting group may be removed without cleaving the peptidomimetic sequence from the solid phase.

The invention further provides a combinatorial library of different sequence peptide or peptidomimetic members synthesized in solution, where each constituent library member includes (a) a peptidomimetic sequence of a combination of three or more amino acid residues and mimics of amino acid residues [bound to solid phase] characterized by (i) a sequence of two or more amino acid residues, mimics of amino acid residues or combinations thereof forming a metal ion-binding domain and including at least one amino acid residue or mimic of an amino acid residue containing at least one S wherein the said S is protected by an orthogonal S-protecting group, (ii) a sequence of one or more amino acid residues, mimics of amino acid residues or combinations thereof at the N- or C- terminus of the metal ion-binding domain, or at both the N- and C-terminus of the metal ion-binding domain; and (b) a unique selection or sequence of amino acid residues, mimics of amino acid residues or combinations thereof in the peptidomimetic sequence of at least one of the constituent members of the library. In this library and the other libraries provided above, the members may include a sequence with at least one amino acid residue or mimic of an amino acid residue containing at least one sulfur atom in which the sulfur atom is protected by a non-orthogonal S-protecting group. In this library and the other libraries provided above, the orthogonal S-protecting group may be removed without removing the non-orthogonal S-protecting group.

In any of the foregoing combinatorial libraries, the metal ion-binding domain can further include at least one N available for binding to a metal ion upon removal of the orthogonal S-protecting group. In one embodiment, the metal ion-binding domain consists of three residues forming an  $N_3S_1$  ligand. The orthogonal S-protecting group may be S-thio-butyl, acetamidomethyl, 4-methoxytrityl, S-sulfonate or 3-nitro-2-pyridinesulfonyl, and the orthogonal S-protecting group may further be removed without otherwise altering the constituent library member. Structural diversity may occur in the metal ion-binding